REMARKS

STATUS OF THE CLAIMS

Claims 1, 8-10, 14-20, 25, 29, 31, 34, 41-43, 47-53, and 58 are pending in the instant application. Claim 34 has been amended. No new matter has been added as a result of such amendment. Claims 1, 8-10, 14-20, 25, 29, and 31 are withdrawn from consideration. Nucleotides 562-648 and 659-688 of SEQ ID NO:1 and nucleotides 3722-3747 of SEQ ID NO:127 as recited in claim 34 are likewise withdrawn from consideration.

CLAIM REJECTIONS UNDER 35 U.S.C. § 102

Claims 34 and 43 are rejected under 35 U.S.C. § 102(e) as being anticipated by US 5,994,076 (hereinafter referred to as "Chenchick"). Specifically, the Examiner states that "SEQ ID NO:1090 is 100% complementary to at least a 9-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1 of Applicant's invention." Applicants respectfully disagree.

Amended claims 34 and 43 are each directed to an antisense compound about 19 to about 23 nucleobases in length. Support for the amendment can be found on page 4, [0035] of the published application (US2008/0194503A1). Chenchick describes methods for analyzing differences in RNA profiles, wherein primers are used to generate labeled nucleic acids from different physiological samples. The primer referred to by the Examiner is a 26mer.

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). Because Chenchick fails to disclose an antisense compound about 19 to about 23 nucleobases in length, it does not anticipate claim 34 or 43. Accordingly, Applicants respectfully request that the present rejection be withdrawn.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103

Claims 34, 41, 43, and 47-49 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US 5,994,076 (hereinafter referred to as "Chenchick") in view of Skerra (*Nucl Acids Res* 1992, 20:3551-3554). Specifically, the Examiner states that "It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an antisense compound 13 to 30 nucleobases in length targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase, wherein said antisense compound is complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID

NO:1 using the teachings and motivation of '076. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the oligonucleotide using the teachings and the motivation of Skerra et al." Applicants respectfully disagree.

As mentioned above, Chenchick describes methods for analyzing differences in RNA profiles, wherein primers are used to generate labeled nucleic acids from different physiological samples. No biological effect is intended for these primers.

Skerra describes an effort to enhance the practical application of thermostable DNA polymerases by preventing exonucleolytic attack on primer molecules via the introduction of single phosphorothioate bonds at the 3' termini. Skerra is, in effect, concerned with the amplification efficiencies of specific polymerases. Skerra makes no mention of compounds with antisense activity or boasting any other biological effect intended for the oligonucleotides, for that matter, beyond as primers for DNA synthesis.

The combination of Chenchick and Skerra fails to provide the person of ordinary skill in the art with any motivation whatsoever to even consider the field of antisense technology. The 1375 primers listed in Chenchick are contemplated for generating labeled nucleic acids to potentially analyze the differences in the RNA profiles between a plurality of different physiological sources. The simple fact that a publication lists 1375 primers used for amplification purposes, of which one is partially complementary to a nucleic acid sequence, cannot be deemed to prompt the person of ordinary skill in the art to contemplate compounds targeting the partially identical nucleic acid sequence as having antisense activity. Any focus by the person of ordinary skill in the art on one of the 1375 primers would be utterly random; Chenchick certainly does not provide any direction or motivation or criteria to follow some selection process to narrow down the unwieldy list of primers.

In marked contrast, the compounds claimed in the instant application are the result of a very focused selection process. The inventors designed and screened 178 oligonucleotides in an effort to identify an effective antisense molecule. Leads were identified by dose response analysis of human p38α mRNA reduction in cells, as well as eliminating sequence motifs known to produce pharmacology by non-antisense mechanisms. IC50 mRNA and target mRNA reduction were investigated in different cell types. Selectivity for the p38α (not β, δ, or γ) isoforms was demonstrated. Specificity for p38α mRNA was then interrogated using homology searches of human gene databases. Finally, a search for single nucleotide polymorphisms in the lead oligonucleotide target sites on the p38α mRNA was performed.

In other words, the instant inventors identified and employed an *extensive* screening process to identify the oligonucleotide compounds and p38α sequence ranges they target, as disclosed in the application (see Examples). The testing done (IC50 mRNA and target mRNA reduction referred to above) demonstrates the screened oligonucleotides' efficacy as antisense compounds. Chenchick and Skerra fail entirely, individually *and* in combination, to provide the person of ordinary skill in the art with any motivation whatsoever to do anything more than generate labeled nucleic acids from samples using primers and compare expression of the labeled nucleic acids in the samples, let alone with an expectation of success to design and screen compounds targeted to a nucleic acid molecule encoding a p38α mitogen-activated protein kinase and demonstrating antisense activity!

Accordingly, Applicants respectfully request that the present rejection be withdrawn.

DOUBLE PATENTING

Claims 34, 41-43, 47-53, and 58 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of US 6,448,079.

Claim 34 has been amended to include the limitation that the recited antisense compound does *not* comprise SEQ ID NO:90, 91, or 92. Thus, Applicants have amended the claim to recite antisense compounds complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1, with the exception of the specific sequences described in '079 and referred to by the Examiner.

The specification describes antisense compounds complementary to at least an 8-nucleobase portion of nucleotides 1194 to 1277 of SEQ ID NO:1. Accordingly, the instant amendment does not present any issues of new matter, since Applicants are simply now claiming less than they have the right to claim. *In re Johnson*, 558 F.2d 1008, 1019 (CCPA 1977)("[the] specification, having described the whole, necessarily described the part remaining.").

If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984).

Indeed, according to the Manual of Patent Examining Procedure (MPEP), the mere absence of a positive recitation is not basis for an exclusion. Furthermore, literal support for

the claimed invention is not required to fulfill the description requirements. *In re Herschler*, 591 F.2d 693, 200 USPQ 711 (CCPA1979); *In re Edwards*, 568 F.2d 1349, 196 USPQ 465 (CCPA1978); *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA1976). Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that Applicants had possession of the concept of what is claimed. *In re Anderson*, 471 F.2d 1237, 176 USPQ 331 (CCPA1973). Indeed, the originally-filed disclosure would have reasonably conveyed to one having ordinary skill in the art that Applicants had possession of the now claimed antisense compounds. *Wang Laboratories, Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767 (Fed.Cir.1993).

Under MPEP 804, "Any obviousness-type double patenting rejection should make clear: (A) The differences between the inventions defined by the conflicting claims - a claim in the patent compared to a claim in the application; and (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue is anticipated by, or would have been an obvious variation of, the invention defined in a claim in the patent." As alluded to above, the Examiner's double patenting rejection is based on her contention that "…the conflicting claims…are not patentably distinct from each other because the antisense compound…" which "…comprises SEQ ID NOs: 90, 91, and 92 claimed in US Patent No. 6,448,079 fully embraces and encompasses the scope of the antisense compound…" as instantly claimed. By excluding the sequences common to '079 and the claimed invention, the conflicting claims are rendered patentably distinct from one another. One skilled in the art would not have been motivated, based on claim 1 of '079, to consider the target region disclosed in amended claim 34. And according to MPEP 806.01, "…it is the claimed subject matter" alone " that is considered and such claimed subject matter must be compared in order to determine the question of distinctness or independence."

Thus, Applicants respectfully request that the Examiner withdraw the present rejection.

CONCLUSION

This constitutes a request for any needed extension of time and an authorization to charge all fees therefor to deposit account No. 19-5117, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to deposit account No. 19-5117.

Respectfully submitted,

/Marina Heusch/

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Marina I. Heusch
Patent Agent #47,647
Swanson & Bratschun, L.L.C.
8210 Southpark Terrace
Littleton, CO 80120
Telephone: (303) 268-0066
Facsimile: (303) 268-0065

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